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EXAMINER	
SPIEGLER, ALEXANDER H	

ART UNIT	PAPER NUMBER
1637	

DATE MAILED: 09/11/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/817,014	REMACLE ET AL.	
	Examiner	Art Unit	
	Alexander H. Spiegler	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 April 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,4,8-10,12-23,38 and 40-45* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,4,8-10,12-23,38 and 40-45* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Status of the Application

1. This action is in response to Paper No. 17, filed on April 28, 2003. Claims 1, 2, 4, 8-10, 12-16, 18-23, and 38 have been amended, Claims 3, 5, 6, 7, 11 and 39 have been canceled, Claims 24-37 have been withdrawn, and Claims 40-45 have been added. Accordingly, Claims 1, 2, 4, 8-10, 12-23, 38 and 40-45 are pending and are rejected.

2. Applicants arguments of Paper No. 17 have been fully considered and thoroughly reviewed. This action is made NON-FINAL because this action contains new rejections not necessitated by Applicants amendments. Any objections and rejections not reiterated below are hereby withdrawn. Specifically, the 103 rejections in the previous action have been withdrawn in lieu of the 103 rejections contained herein. Additionally, the 112, 2nd paragraph rejections have been withdrawn in view of Applicants amendments and arguments.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 1, 2, 4, 8-10, 12-23, 38 and 40-45 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A) Claims 1, 2, 4, 8-10, 12-23, 38 and 40-45 over Claim 1's recitation of "nucleic acid characteristic" because it is not clear as to what encompasses a "nucleic acid characteristic"; this recitation is not defined in the specification, and it is not an art recognized term.

B) Claims 1, 2, 4, 8-10, 12-23, 38 and 40-45 Claim 1's recitation of "said nucleotide sequence" because this recitation lacks antecedent basis. That is, previously, the claim referred to a "nucleotide sequence **characteristic**", not a "nucleotide sequence". Furthermore, Claim 1's recitation of "said homologous nucleotide sequences" and "said amplified or copied nucleotide sequence" also lack antecedent basis because the claim does not previously refer to "homologous nucleotide sequences" or "amplified or copied nucleotide sequences".

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. Claims 1, 2, 4, 8-10, 12-23, 38 and 40-45 rejected under 35 U.S.C. 103(a) as being unpatentable over Brown et al. (USPN 5,807,522), in view of Vannuffel et al. (WO 99/16780, cited in the IDS), and in further view of Bamdad et al. (USPN 6,541,617).

Brown teaches:

"In another aspect, the invention includes a substrate with a surface *having a microarray of at least 10^3 distinct polynucleotide or polypeptide biopolymers in a surface area of less than about 1 cm^2. Each distinct biopolymer (i) is disposed at a separate, defined position in said array, (ii) has a length of at least 50 subunits, and (iii) is present in a defined amount between about 0.1 femtomoles and 100 nanomoles.*

In one embodiment, the surface is glass slide surface coated with a polycationic polymer, such as polylysine, and the biopolymers are polynucleotides. In another embodiment, the substrate has a water-impermeable backing, a water-permeable film formed on the backing, and a grid formed on the film. The grid is composed of intersecting water-impervious grid elements

extending from said backing to positions raised above the surface of said film, and partitions the film into a plurality of water-impervious cells. *A biopolymer array is formed within each well.*

More generally, there is provided *a substrate for use in detecting binding of labeled polynucleotides to one or more of a plurality different-sequence, immobilized polynucleotides.* The substrate includes, in one aspect, a glass support, a coating of a polycationic polymer, such as polylysine, on said surface of the support, and an array of distinct polynucleotides electrostatically bound non-covalently to said coating, where each distinct biopolymer is disposed at a separate, defined position in a surface array of polynucleotides.

Also forming part of the invention is *a method of detecting differential expression of each of a plurality of genes in a first cell type, with respect to expression of the same genes in a second cell type. In practicing the method, there is first produced fluorescent-labeled cDNAs from mRNAs isolated from the two cells types, where the cDNAs from the first and second cell types are labeled with first and second different fluorescent reporters.*

A mixture of the labeled cDNAs from the two cell types is added to an array of polynucleotides representing a plurality of known genes derived from the two cell types, under conditions that result in hybridization of the cDNAs to complementary-sequence polynucleotides in the array. The array is then examined by fluorescence under fluorescence excitation conditions in which (i) polynucleotides in the array that are hybridized predominantly to cDNAs derived from one of the first or second cell types give a distinct first or second fluorescence emission color, respectively, and (ii) polynucleotides in the array that are hybridized to substantially equal numbers of cDNAs derived from the first and second cell types give a distinct combined fluorescence emission color, respectively. *The relative expression of known genes in the two cell types can then be determined by the observed fluorescence emission color of each spot.*" (col. 4)

Additionally, Brown teaches a plurality of uses for the microarray described above, such as "large scale hybridization assays in numerous genetic applications, including genetic and physical mapping of genomes, monitoring of gene expression, DNA sequencing, genetic diagnosis, genotyping of organisms, etc." (col. 14-15, see also Example 3). Brown also teaches the target nucleotide sequence can amplified prior to being hybridized to the capture nucleotide sequences on an array (col. 15), and that the target can be a microorganism (Example 1).

Therefore, Brown teaches methods of identifying and/or quantifying an organism or part of an organism by hybridizing labeled target sequences to capture nucleotide sequences on an

array, wherein the array has a density of at least 4 different bound single stranded capture nucleotide sequences/cm^2.

Brown does not teach the specific detection of a nucleotide sequence that is homologous to at least 4 other nucleotide sequences from other organisms, such as Staphylococci species using consensus sequences from the *femA* nucleotide sequence.

However, Vannuffel teaches the specific detection of Staphylococci species using consensus sequences from the *femA* nucleotide sequence (see abstract). Vannuffel teaches the use of specific primers and probes of the consensus *femA* sequence (pgs. 4, 7 and 8-10). More specifically, Vannuffel teaches a method for identification and/or quantification of at least 4 homologous staphylococcal species comprising, obtaining a staphyoloccal species from a biological sample, possibly purifying and amplifying said sample, and then identifying said species through hybridization on an oligonucleotide array, wherein the consensus sequences of *femA* are used as capture nucleotide sequences (pgs. 11-12). Vannuffel also teaches that the method can be advantageously combined with another specific detection step of possible resistance to antibiotics. Examples 1-7 of Vannuffel further exemplify additional embodiments of the methods outlined above.

In view of the teachings of Vannuffel, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Brown so as to have included the consensus sequences (i.e. primers and probes) specific for the *femA* sequence of Staphylococcal species, in order to have achieved the benefit of providing an effective means of detecting specific species of the Staphylococci genus for use in diagnosing staphylococcal infections, for example.

It is further noted that Brown teaches the use of spacers on the array (e.g., glass slide surface coated with a polycationic polymer, such as polylysine), but Brown does not teach a spacer that is at least 6.8 nm in length.

However, Bamdad teaches "for efficient hybridization of nucleic acids on a surface, the hybridization should occur at a distance from the surface i.e., the kinetics of hybridization increase as a functions of the distance from the surface" (col. 17, ln. 9-13). Bamdad teaches that the closest nucleotide of the nucleic acid can be positioned at least 500 Angstroms from the surface (i.e., the spacer can be a polynucleotide up to 500 Angstroms or 50 nm long) (col. 17, ln. 18-21). It is also noted that Bamdad teaches using arrays (col. 10, ln. 20-31, for example).

In view of the teachings of Bamdad, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Brown so as to have used a spacer of at least 6.8 nm, in order to have achieved the benefits stated by Bamdad of increasing the kinetics of hybridization, thus providing a more efficient means of hybridization/detection.

7. Claim 18 is rejected under 35 U.S.C. 103(a) as being unpatentable over Brown et al. (USPN 5,807,522), in view of Vannuffel et al. (WO 99/16780, cited in the IDS), in view of Bamdad et al. (USPN 6,541,617), as applied to claims 1, 2, 4, 8-10, 12-17, 38 and 40-45 and in further in view of Boon et al. (USPN 6,488,932).

The teachings of Brown, Vannuffel and Bamdad are presented above. Specifically, the references teach the method of identifying or quantifying an organism or part of an organism in a sample by detecting a nucleotide sequence characteristic of said organism, wherein said nucleotide sequence is homologous to at least 4 other nucleotide sequences from other

organisms. The references do not teach the sequence to be identified belongs to the MAGE family.

However, Boon teaches that is advantageous to detect sequences that belong to the MAGE family (which are closely related) for the diagnosis of tumors. (See Fig. 4 and cols. 3-8, for example)

In view of the teachings of Boon, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Brown, Vannuffel and Bamdad so as to have included the steps of detecting a sequence belonging to the MAGE family, in order to have achieved the benefit of providing an effective means of diagnosing a tumor.

8. Claim 19 is rejected under 35 U.S.C. 103(a) as being unpatentable over Brown et al. (USPN 5,807,522), in view of Vannuffel et al. (WO 99/16780, cited in the IDS), in view of Bamdad et al. (USPN 6,541,617), as applied to claims 1, 2, 4, 8-10, 12-17, 38 and 40-45 and in further in view of Apple et al. (USPN 5,451,512).

The teachings of Brown, Vannuffel and Bamdad are presented above. Specifically, the references teach the method of identifying or quantifying an organism or part of an organism in a sample by detecting a nucleotide sequence characteristic of said organism, wherein said nucleotide sequence is homologous to at least 4 other nucleotide sequences from other organisms. The references do not teach the sequence to be identified belongs to the HLA-A family.

However, Apple teaches that is advantageous to detect sequences that belong to the HLA-A family (which are closely related) to help determine potential transplantation donors, thus aiding in minimizing the risk of transplantation rejection. (See cols. 1-8, for example)

In view of the teachings of Apple, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Brown, Vannuffel and Bamdad so as to have included the steps of detecting a sequence belonging to the HLA-A family, in order to have achieved the benefit of providing an effective means of minimizing the risk of transplantation rejection.

9. Claims 20 and 22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Brown et al. (USPN 5,807,522), in view of Vannuffel et al. (WO 99/16780, cited in the IDS), in view of Bamdad et al. (USPN 6,541,617), as applied to claims 1, 2, 4, 8-10, 12-17, 38 and 40-45 and in further in view of Klein et al. (USPN 6,255,059).

The teachings of Brown, Vannuffel and Bamdad are presented above. Specifically, the references teach the method of identifying or quantifying an organism or part of an organism in a sample by detecting a nucleotide sequence characteristic of said organism, wherein said nucleotide sequence is homologous to at least 4 other nucleotide sequences from other organisms. The references do not teach the sequence to be identified belongs to the dopamine or histamine receptors coupled to the G genes family.

However, Klein teaches that is advantageous to detect sequences that belong to the dopamine or histamine receptors coupled to the G genes family (which are closely related) to mediate transmembrane signaling by external stimuli, endocrine function, carbohydrate metabolism, etc. (See cols. 1-4, for example)

In view of the teachings of Klein, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Brown, Vannuffel and Bamdad so as to have included the steps of detecting a sequence belonging to the dopamine or

histamine receptors coupled to the G genes family, in order to have achieved the benefit of providing an effective means of mediating transmembrane signaling for many vital biological processes, such as carbohydrate metabolism.

10. Claim 21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Brown et al. (USPN 5,807,522), in view of Vannuffel et al. (WO 99/16780, cited in the IDS), in view of Bamdad et al. (USPN 6,541,617), as applied to claims 1, 2, 4, 8-10, 12-17, 38 and 40-45 and in further in view of Murphy et al. (WO 94/05695).

The teachings of Brown, Vannuffel and Bamdad are presented above. Specifically, the references teach the method of identifying or quantifying an organism or part of an organism in a sample by detecting a nucleotide sequence characteristic of said organism, wherein said nucleotide sequence is homologous to at least 4 other nucleotide sequences from other organisms. The references do not teach the sequence to be identified belongs to the choline receptors coupled to the G genes family.

However, Murphy teaches that is advantageous to detect sequences that belong to the choline receptors coupled to the G genes family (which are closely related) for use in diagnosis of neurological, viral or endocrine pathologies. (See pgs. 12-16 and 26-34, for example)

In view of the teachings of Murphy, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Brown, Vannuffel and Bamdad so as to have included the steps of detecting a sequence belonging to the choline receptors coupled to the G genes family, in order to have achieved the benefit of providing an effective means of diagnosing neurological, viral or endocrine pathologies.

Applicants Arguments

11. In Paper No. 17, Applicants argued the references did not teach an array comprising a spacer that is at least 6.8 nm. However, this argument is not persuasive in view of the teachings of Bamdad, which specifically teaches the advantages of using spacers that are at least 6.8 nm in hybridization assays (see above).

Conclusion

12. No claims are allowable.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Alexander H. Spiegler whose telephone number is (703) 305-0806. The examiner can normally be reached on Monday through Friday, 7:00 AM to 3:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (703) 308-1119. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 and (703) 305-3014. Applicant is also invited to contact the TC 1600 Customer Service Hotline at (703) 308-0198.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Alexander H. Spiegler
September 2, 2003

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